

January 10, 1950.

Dr. C. C. Lindegren,
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Carbondale, Illinois.

Dear Carl-

I promised that I would write you in more detail to press my suggestion that the hybrid diploids should be examined for their fermentative phenotypes in certain crosses.

This experiment would be most instructive in crosses of a standard fermenter with a recessive, non-fermenting converter stock, and would have, as its primary aim, the determination of whether the "convertible" dominant gene is lost only at meiosis, or whether its loss can already be detected in diploid cells before sporulation. Of course, it will be necessary to avoid sporulation in the cultures, but I understand that you know how to do this quite effectively. Probably it is best to approach this experiment merely to get additional information on the mechanism and conditions of conversion.

The experiment should involve a mass mating, and the isolation of diploid clones immediately, and following an interval of mitotic proliferation. It should then be determined whether a) diploid clones lacking any of the dominant characters will occur, and b) a diploid which is verified as possessing the dominant phenotype will give some asci all spores of which are recessive. The latter can easily be done by ~~inoculating~~ using entire asci to start cultures, provided reasonably complete germination can be assured. If nothing else, I think that it might be very important to determine whether some diploids from a given cross throw off many converted asci, while others do not, or whether ~~all other diploids~~ of a given mating have the same potentiality for producing converted asci.

(In this sense, this is not a very critical expt.) I think that you will agree that your conversion theory would predict that the diploid clones should be phenotypically dominant, and that conversion occurs at meiosis, although it would be easy enough to accommodate the alternative finding (i.e. recessive phenotypes) with a slight modification of the conversion theory. If the latter is true, however, (i.e. conversion in the diploid), I think that it might be necessary to accept the position that the yeasts show a rather exceptional behavior, because this type of conversion might just as well be detected without the advantages of tetrad analysis. I will admit that genetic material is selected

for segregation in the F2. However, this type of conversion is formally very similar to cytoplasmic inheritance (I don't mean a difference in reciprocal crosses, but just the blending- toward the converting type - and lack of subsequent segregation), and I suspect that this has been rather extensively looked for. Perhaps it has been hidden under the name of modifiers or polygenes or whatnot, but at any rate you could point out what should be looked for if this is the pattern. On the other hand, if conversion does not take place in the diploid, but only at meiosis, you might be verifying your argument considerably, although as we agreed the final answers are going to depend on thorough maps with lots of closely linked markers,

Esther and I enjoyed very much seeing you again, and were only sorry that you hadn't dragged Gerry out of the lab and along with you.

Sincerely,

Joshua Lederberg.